Apparatus for Stacking, Repositioning, Agitating and Knocking

Statement of Related Cases

[0001] This case claims priority of U.S. Provisional Patent Application Serial No. 60/430,255, filed December 2, 2002.

Field of the Invention

[0002] The present invention relates to an apparatus for performing operations that are required or otherwise desirable in conjunction with growing cells within a cell-cultivating flask.

Background of the Invention

[0003] Developments in cellular biology and related fields have led to increased demands for devices capable of producing cells. The cells are often used, for example, to produce biologically-active compounds.

[0004] For growing static cell cultures, flat, flask-like containers ("cell-cultivating flasks") are typically used. The flasks usually incorporate a neck and an opening that is closed using a screw cap. Some flasks in the prior art incorporate internal structures for cultivating the cells, while others do not.

[0005] After adding a cultivating medium and cells to the flask, it is sometimes necessary to conduct certain physical operations. These operations include, for example, changing the orientation of the flask (*e.g.*, from a horizontal position to a vertical position, or visa-versa, *etc.*) and agitating the flask. Furthermore, on the completion of cell growth, and prior to emptying the cell-cultivating flasks, it is sometimes necessary to "knock" or shake the flask to loosen cellular material that otherwise adheres to the internal walls of the flask.

[0006] Traditionally, these physical operations have been performed manually. Such manual operations limit production and increase production expenses. As a consequence, the art would benefit from an apparatus that can automatically perform these operations.

Summary

[0007] The illustrative embodiment of the present invention is an apparatus that is capable of performing at least some of the physical operations that are used in

conjunction with growing cells in cell-cultivation flasks. The physical operations performed by an apparatus in accordance with the illustrative embodiment include one or more of the following functions, in addition to any others:

- Receiving, in a stack, a plurality of cell-cultivation flasks, wherein the flasks can be fed manually or by a robotic system to the apparatus.
- Re-orienting the flasks from a horizontal position to a vertical position or visa versa.
- Agitating liquid within the flasks, advantageously creating a circular flow of liquid.
- "Knocking" the cell-cultivation flasks to loosen cellular material within the flasks.

[0008] In accordance with the illustrative embodiment, horizontal-to-vertical re-positioning is implemented using a movable platform that cooperates with guides. In use, cell-cultivating flasks are stacked on the movable platform.

[0009] In the illustrative embodiment, the guides are implemented as slots in a frame. More particularly, in some embodiments, the frame includes two, spaced plates, each of which has a generally horizontal base and a generally vertical riser, wherein the riser depends from one end of the base. A slot is defined in both the base portion and the riser portion of each plate.

[0010] The slot in the base is horizontal, while the slot in the riser takes the form of a vertical arc. In the illustrative embodiment, two sets of rollers depend from the platform; one set (proximal to a first end of the platform) engages the slot in the base and the other set (distal to the first end of the platform) engages the slot in the riser. Moving the platform towards the riser causes the set of rollers that cooperate with the slot in the riser to ride upwards in a vertical arc. This causes the second end of the platform to move upward. Since the first end of the platform does not move in the vertical direction due to its engagement with the horizontal slot, the platform rotates about the first end toward a vertical orientation. The motion of the platform is actually a combination of sliding and rotating, since the platform moves horizontally toward the riser while the second end rises. With continued movement toward the riser, the platform attains full vertical orientation, having rotated ninety degrees from its horizontal orientation. Cell-cultivating flasks that are stacked on the platform are, of course, rotated along with the platform.

[0011] The use of the slotted frame and cooperating movable platform, in accordance with the illustrative embodiment, enables the apparatus to maintain the same bottom reference plane. That is, at least part of the movable platform is always engaged to horizontal slot in the base, which defines a bottom reference plane. This is in contrast to a classic mechanism for rotating an object, which utilizes a "twisting" action. The classic mechanism typically does not maintain the bottom reference plane, and, in fact, has to be lifted to enable an object to be rotated (assuming that the object is resting upon a surface).

[0012] In accordance with the illustrative embodiment, the slot in the riser of one of plates and a slot in the base of the other of the two plates include a deviated portion. The deviated portion causes a local change in the height of slots. Moving the movable platform back-and-forth such that it successively passes the deviated portions in the two slots causes a wobbling motion in the platform — and in any cell-cultivating flasks that are disposed on the platform. This wobbling motion places liquid within the flasks in orbital (*i.e.,* circular) motion.

[0013] The slots in the frame are, therefore, dual functional, in the sense that they enable both the re-positioning and agitation functions. And as a consequence of this dual functionality, a single actuator can be used to drive both the re-positioning and agitating operations.

[0014] In some embodiments, the apparatus also incorporates a spring-loaded "hammer" mechanism that generates an adjustable and repeatable force (a "knocking") that is directed against the side of the cell-cultivating flasks. In some embodiments, the spring-loaded hammer is implemented as a passive device, wherein the energy that loads the spring is imparted by the actuator that drives the re-positioning (and agitating) operation. An embodiment of the spring-loaded "hammer" mechanism is described in applicant's co-pending patent application entitled "Passive Force-Imparting Mechanism" (Attorney Docket No. 153-035, filed 02 December 2003), incorporated by reference herein.

Brief Description of the Drawings

[0015] **FIG. 1** depicts an apparatus **100** in accordance with the illustrative embodiment of the present invention, wherein a plurality of cell-cultivating flasks, which are stacked on the apparatus, are in a horizontal orientation.

[0016] **FIG. 2** depicts the apparatus of FIG. 1, wherein the cell-cultivating flasks are in a vertical orientation.

[0017] **FIG. 3** depicts the apparatus of FIG. 1, but without cell-cultivating flasks present. Furthermore, FIG. 3 depicts drive mechanism **330** of apparatus **100**.

[0018] **FIG. 4** depicts the apparatus of FIG. 3.

[0019] **FIG. 5** depicts a flow of liquid within a cell-cultivating flask during agitation.

Detailed Description

[0020] FIG. 1 depicts apparatus **100**, which includes frame **102** and platform **118**, which cooperate as depicted.

[0021] In the illustrative embodiment, frame **102** comprises two, identical plates **104**. Each plate **104** has a generally horizontal base **106** and a generally vertical riser **108**. The riser depends from base **106** near one end thereof. In some embodiments, bases **106** are attached to an underlying platform, which is not depicted. The underlying platform can be used, for example, to support a spring-loaded hammer mechanism to implement a knocking operation.

[0022] Each base **106** includes slot **110**, which has a substantially horizontal orientation. Each riser **108** includes arcuate-shaped slot **114**, which has a substantially vertical orientation. As used herein, the term "**substantially horizontal orientation**" means a near-horizontal orientation of the slot, such as 0 degrees +/- about 5 degrees. As used herein, the term "**substantially vertical orientation**" means that, relative to the horizontal (*e.g.*, relative to slot **110**), slot **114** is angled upwards at an angle of at least about 45 degrees (wherein the angle is defined by two intersecting rays, one of which is coincident with slot **110** and the other of which passes through the end points of slot **114)**.

[0023] Slot **110** in base **106** of one of plates **104** includes deviated portion **112**. Vertically-oriented slot **114** in riser **108** of the other of plates **104** includes deviated portion **116**. (Only deviated portion **112** is visible in FIG. 1; *see* FIGs. 4 and 5 for deviated portion **116**.)

[0024] In the illustrative embodiment, deviated portion **112** is displaced upward relative to the rest of slot **110** and deviated portion **116** is displaced upward relative to the immediately surrounding portion of slot **114**. In some other embodiments (not depicted), each deviated portion **112,116** is displaced downward. As described

more fully later in this specification, deviated portions **112** and **116** are used during agitation operations to impart circular motion to a liquid being agitated within cell-cultivating flasks **126**.

[0025] Platform **118** receives cell-cultivating flasks **126**. In the illustrative embodiment, platform **118** includes retainer **120**, which depends from the front end of the platform (*i.e.*, the "right" end as viewed in FIG. 1). As described further below, retainer **120** is used in conjunction with re-positioning operations.

[0026] Platform **118** is movable relative to frame **102** to facilitate re-positioning and agitating operations. In the illustrative embodiment, platform **118** is physically adapted to slide within frame **102**. This capability is provided, in the illustrative embodiment, by two sets of rollers that cooperate with slots **110** and **114**. More particularly, platform **118** includes a set of front rollers **122** and a set of rear rollers **124**. Front rollers **122** engage and are guided by slots **110** in bases **106**. Similarly, rear rollers **124** engage and are guided by slots **114** in risers **108**.

[0027] The cooperating arrangement of rollers **122**, **124** and slots **110**, **114** are sufficient to keep plates **104** of frame **102** in spaced, parallel relation to one another. In some variations of the illustrative embodiment (not depicted), individual sections **104** are linked to one another at risers **108** by one or more beams to provide additional rigidity.

[0028] As indicated above, in use, one or more flasks **126** are loaded onto platform **118**. Flasks **126**, which in the illustrative embodiment are flat flasks, each include a port, which will typically having a protruding "neck" or "throat" for receiving liquid. (Not depicted in FIG. 1, *see*, FIG. 2: "ports 228".) FIG. 1 depicts six flasks **126** on platform **118**, although a greater number or less number of flasks can be accommodated. The flask loading operation can be conducted either manually or automatically, in conjunction with materials-handling equipment (not depicted).

1. Re-positioning Function

[0029] With reference to FIG. 2, re-orientation (vertical positioning) of flasks **126** is achieved by forcing platform **118** towards the rising curve of slots **114** until both rear rollers **124** and front rollers **122** reach their limits of travel. When flasks **126** are in a vertical position, ports **228** are oriented "upwards" to be accessed by a fluid-delivery mechanism. (The fluid-delivery mechanism is not a part of this invention

and is not described or depicted herein.) Retainer **120** supports plates **126** when platform **118** is in a vertical position.

[0030] Platform **118** is moved via a drive mechanism, which can be implemented in many different ways. In the illustrative embodiment depicted in FIG. 3, drive mechanism **330** is implemented as a linear actuator. The linear actuator is realized, in the illustrative embodiment, as an air-actuated piston/cylinder.

[0031] Drive mechanism **330** is secured to a surface or platform that underlies bases **106** of frame **102**. Piston **332** of drive mechanism **330** is coupled to front (right) end of platform **118** (*i.e.*, near retainer **120**). Drive mechanism **330** is appropriately positioned so that as piston **332** is retracted in direction **333** into cylinder **334**, platform **118** moves toward generally vertically-oriented slots **114**. As it does so, rollers **124** ride up slots **114** and rollers **122** travel toward the back of slots **110**. This movement re-positions platform **118** and any flasks **126** that are disposed on it, into the vertical orientation depicted in FIG. 2.

[0032] Thus, in the illustrative embodiment, slots **110** and **114** in respective x and z planes convert the linear and horizontal movement of drive mechanism **330** into rotational movement of platform **118**.

2. Agitation Function

[0033] Any liquid that is present in flasks **126** can be agitated by moving platform **118** back and forth in a reciprocating motion. Furthermore, by virtue of deviated portions **112** and **116**, such liquid can advantageously be agitated into circular wave motion.

[0034] Referring now to FIGs. 4 and 5, moving platform **118** back and forth along vector **436** using drive mechanism **330** will cause liquid to move back and forth in wave motion within flasks **126**. FIG. 5 depicts path **546** of liquid within a flask **126**.

[0035] As platform **118** begins to move toward the "right" along direction **446** (FIG. 4), liquid flows along path **546** toward the "right" side of flask **126** (FIG. 5). As platform **118** moves further rightward, roller **122** rides up deviated portion **112** of slot **110**. This causes "forward" right corner **438** of platform **118** to rise relative to "rearward" right corner **440**. Consequently, platform **118** is tilted toward corner **440**. As depicted in FIG. 5, this causes liquid within flask **126** to move from relatively-higher corner **538** to relatively-lower corner **540** along path **547**.

[0036] As platform **118** begins to move back toward the left along direction **448** (FIG. 4), liquid flows toward the "left" side of flask **126** along path **548** (FIG. 5). As platform **118** moves further leftward, roller **124** rides up deviated portion **116** of slot **114**. This causes "rearward" left corner **442** to rise relative to "forward" left corner **444**. Consequently, platform **118** is tilted toward corner **444**. As depicted in FIG. 5, this causes liquid within flask **126** to move from relatively-higher corner **542** to relatively-lower corner **544** along path **549**.

[0037] In this fashion, circular wave motion is created in flasks **126**. This agitation pattern can be advantageous as a function of the particular processes that are occurring within flasks **126**.

[0038] It is to be understood that the above-described embodiments are merely illustrative of the present invention and that many variations of the above-described embodiments can be devised by those skilled in the art without departing from the scope of the invention. It is therefore intended that such variations be included within the scope of the following claims and their equivalents.